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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,840	02/27/2004	Thomas J. Meade	A-67277-5/RMS/RMK	8243

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EXAMINER	
SAMALA, JAGADISHWAR RAO	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
06/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,840	MEADE, THOMAS J.	
	Examiner	Art Unit	
	JAGADISHWAR R. SAMALA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,10-15 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,10-15 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 February 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of amendment filed on 12/10/2007. Upon entering the amendment, the claims 10 and 17 are amended. Accordingly, claims 1-4, 10-15 and 17 are pending and have been examined on the merits for patentability.

Terminal Disclaimer

2. The terminal disclaimer filed on 12/10/2007 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US 6,713,046 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Priority

3. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. US 09/179,927 (now US 6,713,046), which claims benefit to US 60/063,328, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Even though the US 60/063,328 document defines the enzyme targets as “enzymes associated with the generation or maintenance

of arterioschlerotic plaques and lesions within the circulatory system, inflammation, wounds, immune response, and tumors, all tumors are basically not cancerous tumors. As such, the priority date for the full scope of instant claims was determined to be the filling date of the US 60/201,817 application, or 05.04./2000.

Response to Arguments

3. Applicant's arguments filed on 12/10/2007 with respect to claims 1-4, 10-15 and 17 have been fully considered but they are not persuasive. The 102(e) rejection of Snow et al (US 5,932,188) is maintained and made FINAL.

Previous rejections that are not reiterated herein are withdrawn.

Claim Rejections - 35 USC § 102

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

1. Claims 1-4, 10-15 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Snow et al. (US 5,932,188).

Snow discloses that, the concept of drug targeting has gained importance in recent years, especially for anticancer drugs, inasmuch as toxic side effects of

anticancer drugs to normal cells are a primary obstacle in cancer chemotherapy due to the lack of selectivity to cancer cells. Reactive poly(alkylene oxides) can be contacted with chelating agents or precursors thereof containing reactive functionality to form targeting polymers which, when associated with cytotoxic agents, find particular utility in therapeutic and diagnostic imaging compositions and methods (column 1, lines 25 - 60). The cytotoxic agent is an agent able to kill cells, including chemotherapeutic agents, which can be covalently bound to a chelating agent or to a linking group. The inherent cytotoxic properties of the agent are maintained or regenerated as a result of cleavage of said bonds (column 2, lines 42+). Preferred residues of chelating agents include DOTA (column 4, lines 35+). Regarding claims 12 - 14, the residue of the chelating agent is linked to the polymer through a chemical bond or linking group, which include a nitrogen atom, alkyl group, including those containing from 1 to 18 carbons being interrupted by one or more heteroatoms, such as oxygen (column 5, lines 47+).

The cytotoxic agent may include doxorubicin (column 7, line 39). The polymer may include both a therapeutic moiety and a moiety for enhancing contrast during MR imaging. For MR imaging applications, the metal ion chelated by the chelator ($M^{+}a$) may include Cr3÷, Fe3÷, Gd3÷, Dy3÷ (column 8, lines 51+). The cytotoxic agents are covalently linked to the polymer or the chelating group or to elements of the linking group by a variety of chemical bonds or linking groups (column 11, lines 9 - 15). In some embodiments, the polymer can contain an immunoreactive group covalently bonded thereto. Such an immunoreactive group has a capacity for interaction with another component which may be found in biological fluids or associated with cells to be

treated such as tumor cells, and may include polysaccharides, carbohydrates, etc. (column 11, lines 60 - column 12, line 16). The compositions can be administered orally, intravenously, etc. (column 14, line 35).

Regarding claim 1, a composition comprising a chelator and a paramagnetic metal ion for MR imaging, a poly(alkylene oxide) polymer, a linker and a cytotoxic agent are be administered. The composition must inherently comprise a "cleavage site" and thus a cleavage step upon in vivo administration, as claimed, because Snow teaches that the inherent cytotoxic properties of the cytotoxic agent are maintained or regenerated as a result of cleavage of covalent bonds which link the cytotoxic agent to the chelating agent, linker, or polymer (column 2, lines 42+). The recitation of such functional properties, such as a decrease in the T_1 of the MRI agent, must also necessarily occur, since the same compositions must have the same properties. Regarding claims 10 and 17, the composition may further comprise a polysaccharide or Carbohydrate group, and thus must inherently be "capable of' being cleaved by a-carbohydrate, as Claimed. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or composition as that which is claimed, the properties applicant discloses and/or claims are necessarily present. See In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Applicant's arguments filed on 12/10/2007 have been fully considered but they are not persuasive.

Applicant asserts that Snow et al does not disclose the cleavage of the bond between the cytotoxic agent and the remaining composition following administration of the compound or subsequence change in T_1 of the chelator.

This argument is not persuasive since Snow does teaches that the cytotoxic agents are covalently bonded to the polymer at one or more sites of attachment, and the inherent cytotoxic properties of the agent being maintained or regenerated as a result of cleavage of said bond or bonds. The recitation of such functional properties, such as a decrease in the T_1 of the MRI agent, must also necessarily occur, since the same composition must inherently have the same properties (see col. 2 lines 50+).

Applicant also asserts that Snow does not disclose a blocking peptide that is cleavable by the target enzyme to produce a change in T_1.

This argument is not persuasive since Snow discloses that the residue of the chelating agent is linked to the polymer moiety through a chemical bond or a linking group, i.e., L and L1 in formula I. Preferred linking groups include amino acid linkage, peptide linkage group, and since the cytotoxic properties of the cytotoxic agent are maintained or regenerated as a result of cleavage of said bond or bonds, when administered for treating disease sites in a patient or a specimen from the patient an effective amount of the polymer the composition would inherently produce a change in T_1.

Conclusion

1. No claims are allowed at this time.

2. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAGADISHWAR R. SAMALA whose telephone number is (571)272-9927. The examiner can normally be reached on 8.30 A.M to 5.00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

Jagadishwar R Samala
Examiner
Art Unit 1618

sjr